DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 09/11/2008 wherein claims 1 and 27 have been amended have been amended and claims 11 and 17 have been cancelled and claims 30-32 are newly added.

2. Claims 1-8 and 10, 12-16 and 18-32 are pending and presented for examination on the merits. The following rejections are made.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. **Claims 1-8, 10, 12-13, 16 and 18-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLaren et al. (US 6039974; of record) in view of Uemura et al. (US 4695467; of record) and Stainforth et al. (US 5858412; of record)**.

5. MacLaren teaches a pharmaceutical composition that is a combination of piperidinoalkanol-decongestant wherein the composition is in the form of a bilayer tablet comprising two discrete zones (see abstract). It is taught formulation A is sustained release portion which comprises a decongestant (i.e. sympathomimetic drug; see instant claims 1 and 27), specifically that of pseudoephedrine which is present in an amount of 120 mg (see column 2,

lines 32-40 and Table 1; see instant claims 2, 3 and 29). Table 1 teaches that the sympathomimetic drug containing layer contains a carnuba wax, stearic acid and silicon dioxide.

6. Formulation B is an immediate release portion which comprises a piperidinoalkanol compound, specifically that of fexofenadine which is present in an amount of 60 mg (see column 2, lines 32-40 and Table 1; see instant claims 1, 4-7 and 29). Fexofenadine is a widely used antihistamine, antiallergic agents and bronchodilator. Table 5 teaches that the fexofenadine containing portion of the tablet comprises among other ingredients a diluent (or filler), a disintegrant and a lubricant which are microcrystalline cellulose (functionally equivalent to lactose (see column 11, line 35)) from about 27% and 73%, croscarmellose sodium from about 0.25% and 6.0% by weight and magnesium stearate from about 0.25% to about 2.00%, respectively (see abstract; see instant claims 1, 12, 13, 16, 18, 24, 25 and 26).

7. It is also taught that Formulation A and Formulation B may contain excipients which are commonly used in the art such as binders, diluents, lubricants, glidants, disintegrants, etc.. It is taught that lubricant may be magnesium stearate and the diluent (or filler) may be lactose (see column 11, lines 20-40; see instant claim 9). MacLaren also teaches that the bilayertblet may be coated (see Table 1).

8. Maclaren fails to teach the sustained release portion, Formulation A, as comprising ethylcellulose from about 10% to about 35% by weight. Maclaren also fails to teach the composition as comprising a filler from about 5% to about 20%, a cellulose binder at a weight percentage from about 20% to about 50%, and from about 2% to about 50% of a wax and a lubricant from about 0.5% to about 2%.

9. The teaching of Uemura is directed to a sustained release tablet formulation. The sustained release formulation comprises granules comprising a drug, a disintegrating agent and a water soluble polymer (see abstract). Example 3 teaches a formulation for a sustained release formulation which comprises a drug, low substituted hydroxypropyl cellulose (binder) at a weight percentage of 23%, hydroxypropyl methylcellulose (binder), lactose (filler) at a weight percentage of 7.5%, carnuba wax (wax) at a weight percent of 25% and magnesium stearate (lubricant) at a weight percent of 0.2% (see instant claims 18-22).

10. Stainforth is drawn to sustained release formulations utilizing pharmaceutical excipients having improved compressibility. It is disclosed that suitable materials for use in sustained release tablet formulations includes alkylcelluloses such as ethylcellulose (see column 16, lines 50-55). It is taught that the tablet will preferably contain the alkyl cellulose between from about 1 to about 80% by weight of the sustained release dosage form (see column 18, line 20; see instant claims 1, 18 and 27).

11. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of MacLaren, Uemura and Stainforth with a reasonable expectation for success in arriving at a bilayer tablet comprising two discrete zones wherein discrete zone A is a sustained release zone which comprises 120 mg of pseudoephedrine and a filler (lactose), a cellulose binder (hydropropyl methylcellulose), ethylcellulose, between 2% to about 50% a wax (carnuba) and a lubricant (magnesium stearate) and wherein discrete zone B is an immediate release zone which comprises 60 mg of fexofenadine, a sugar (lactose), disintegrant (croscarmellose sodium) and a lubricant (magnesium stearate) at the required weight percentages (see above). The significance of MacLaren is that it teaches the major inventive

concept, a bilayer tablet in which one layer is a sustained release layer for psuedoephedrine and the other layer is an immediate release layer for fexofenadine wherein the fexfenadine layer further comprises a cellulose diluent, a disintegrant and a lubricant. Moreover, MacLaren teaches that the cellulose diluent (microcrystalline cellulose) is functionally equivalent to lactose (see above) as well as indicates that both portions of the tablet may include excipients such as lactose and magnesium stearate. MacLaren fails to teach portion A of the tablet comprising a filler, a cellulose binder, ethylcellulose, a wax and a lubricant at the specified weight percentages (see above). With respect to the inclusion of a wax from about 2 to 50% and the inclusion of a cellulose binder, a lubricant and a filler, the teaching of Uemura cures these deficiencies. Uemura teaches a formulation for a sustained release tablet comprising a cellulose binder, specifically low-substituted hydroxypropyl cellulose at a weight percentage of 23%, lactose at a weight percentage of 7.5%, a wax at a weight percentage of about 25%. With respect to the inclusion of ethylcelluose, the teaching of Stainforth cures this deficiency. Stainforth states that ethylcellulose is a commonly used carrier matrix in sustained release tablet formulations and can be used between 1-80 weight %. As all of these references are within the same general field of endeavor (i.e. adjusting the rate of release from a solid dosage form), one would have been motivated to combine the references and arrive at a product possessing the instantly claimed properties. It should be noted that the excipients which Applicant employs in their dosage forms are commonly used in tablet formulations (both immediate and sustained release formulations), and it would have been obvious to one ordinarily skilled in the art to adjust and vary the amounts of the ingredients in the composition to arrive at a dosage form with the greatest therapeutic properties. Therefore, the invention as a whole is *prima facie* obvious to one ordinary skill in the

art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

12. **Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over MacLaren et al. (US 6039974; of record) in view of Uemura et al. (US 4695467; of record), Stainforth et al. (US 5858412; of record) and Okada et al. (US 5164193; of record)**.

13. Maclaren, Uemura and Stainforth are relied upon for disclosure described in the rejection of claim 1-8, 10, 11-13, 16 and 18-29 under 35 U.S.C. 103(a).

14. MacLaren, Uemura and Stainforth fail to teach the sustained release portion of the bilayer tablet (A) as comprising between 2% to about 50% stearyl alcohol.

15. Okada cures this deficiency. Okada is drawn to a sustained release tablet which comprises an oil or waxy component (see abstract). Many oily and waxy components are disclosed (see column 2 and column 3) such as carnuba wax and stearyl alcohol. It is disclosed that stearyl alcohol is a preferred alcohol (see column 3, line 20). Moreover, it is taught that in order to ensure the effect of the present invention that the oil component bet present a weight percentage of 5.0% and greater (see column 4, line 10).

16. Therefore, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to combine the teachings of MacLaren, Uemura, Stainforth and Okada with a reasonable expectation for success in arriving at a bilayer tablet in which the sustained release (A) portion comprises lactose (see above), hydroxypropylmethylcellulose (see above), ethylcellulose (see above), stearyl alcohol at about 5.0 wt. % or more and magnesium stearate (see above). The significance of Okada is that it teaches stearyl alcohol as being a particularly

preferred and a useful oily component for implementation in a sustained release formulation. Moreover, it is taught that carnuba wax is functionally equivalent to stearyl alcohol. One of ordinary skill in the art would be motivated to substitute one for the other with a reasonable expectation for success in a product having sustained release properties. Therefore, a composition sustained release layer of a bilayer tablet comprising about 5% stearyl alcohol is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

17. **Claims 14, 15 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLaren et al. (US 6039974; of record) in view of Uemura et al. (US 4695467; of record), Stainforth et al. (US 5858412; of record) and Bertelsen et al. (US 6713089; of record).**

18. Maclaren, Uemura and Stainforth are relied upon for disclosure described in the rejection of claim 1-8, 10, 11-13, 16 and 18-29 under 35 U.S.C. 103(a).

19. MacLaren, Uemura and Stainforth fails to teach the immediate release portion of the bilayer tablet (B) as comprising the disintegrant low-substituted hydroxypropyl cellulose wherein the low-substituted hydroxypropyl cellulose may be selected from a wide range of species with varying hydroxypropy content and average particle size.

20. Bertelsen is drawn to rapid release formulations. It is disclosed that low-substituted hydroxypropyl cellulose is a useful disintegrant (see column 14, lines 35-55; see instant claim 14). Exemplified low-substituted hydroxycellulose include LH-20 and LH-21 (see column 14, line 55; see instant claim 15).

21. Therefore, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to combine the teachings of MacLaren, Uemura, Stainforth and Bertelsen with a reasonable expectation for success in arriving at a bilayer tablet in which the immediate release portion (B) comprises the disintegrant low-substituted hydroxypropyl cellulose (i.e. LH-20 or LH-21), a filler (lactose, see above) and a lubricant (magnesium stearate, see above). The significance of Bertelsen is that it teaches the inclusion of low-substituted hydroxypropyl cellulose in a rapid release formulation which has a disintegrant function. Thus, one would have been motivated to use a low-substituted hydroxypropyl cellulose compound in a rapid release composition or rapid release portion of a bilayer tablet with a reasonable expectation for success for that composition to possess rapid release properties. Therefore, a bilayer tablet which comprises a immediate release layer comprising low-substituted hydroxypropyl cellulose is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

22. **Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over MacLaren et al. (US 6039974; of record) in view of Uemura et al. (US 4695467; of record), Stainforth et al. (US 5858412; of record), Okada et al. (US 5164193; of record) and Bertelsen et al. (US 6713089; of record)**.

23. Maclaren, Uemura, Stainforth and Okada are relied upon for disclosure described in the rejection of claim 30 under 35 U.S.C. 103(a).

24. MacLaren, Uemura, Stainforth and Okada fail to teach the immediate release portion of the bilayer tablet (B) as comprising as the disintegrant low-substituted hydroxypropyl cellulose.

25. Bertelsen is drawn to rapid release formulations. It is disclosed that low-substituted hydroxypropyl cellulose is a useful disintegrant (see column 14, lines 35-55; see instant claim 14). Exemplified low-substituted hydroxycellulose include LH-20 and LH-21 (see column 14, line 55; see instant claim 32).

26. Therefore, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to combine the teachings of MacLaren, Uemura, Stainforth, Okada and Bertelsen with a reasonable expectation for success in arriving at a bilayer tablet in which the immediate release portion (B) comprises as the disintegrant low-substituted hydroxypropyl cellulose. The significance of Bertelsen is that it teaches the inclusion of low-substituted hydroxypropyl cellulose in a rapid release formulation which has a disintegrant function. Thus, one would have been motivated to use a low-substituted hydroxypropyl cellulose compound in a rapid release composition or rapid release portion of a bilayer tablet because Maclaren specifically stipulates for the inclusion of a disintegrant component. One would be motivated to scour the art in search of compounds capable of performing Maclarens intended purpose. Therefore, a bilayer tablet which comprises a immediate release layer comprising low-substituted hydroxypropyl cellulose is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
October 20, 2008

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611